

# Thermoreversible hydrogel-coated microneedles for dermal drug delivery

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## Introduction

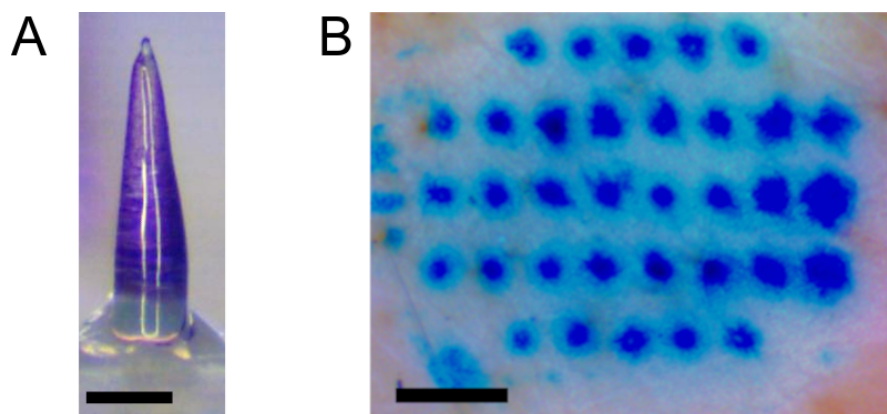
Drug-coated microneedle patches are a minimally invasive technique for dermal drug delivery. However, their formulation usually requires careful calibration of formulation viscosity to enable fluid flow through the coating equipment at a sufficiently low viscosity, yet promote bulk formation on the microneedle surface at a sufficiently high viscosity [1, 2]. Clearly, an ability to manipulate the viscosity of the coating formulation during the coating process will be advantageous. Here, we evaluate thermoreversible hydrogel formulations as a strategy to do so, using temperature as a trigger.

## Materials and methods

Methylene blue (MB, 0.5% w/w) was formulated as a model drug in poloxamer 407 (15–28% w/w) hydrogels. Sol-gel transitions were determined using rotational rheometry. Microwells for dip-coating were produced from polydimethylsiloxane against a 3D-printed negative template. Cold liquid MB-poloxamer formulations were pipetted into microwells and warmed at 30°C until gelling. Polylactic acid microneedles were fabricated by micromoulding [3] and dipped into the gelling MB-poloxamer formulations. MB loading and in vitro release were quantified using UV/Vis spectrophotometry ( $\lambda = 665$  nm). Coated microneedles and MB release in excised porcine skin were visualised by light microscopy.

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**Figure 1:** (A) A microneedle coated with MB-poloxamer hydrogel formulation, and (B) En face image of skin, captured 15 min after microneedle insertion, showing MB released from a microneedle patch coated with a MB-poloxamer formulation. Scale bars: (A) 200  $\mu\text{m}$ , (B) 2 mm.

## Results and discussion

The MB-poloxamer formulations underwent reversible sol-gel transitions between 10–25°C. MB incorporation did not alter the sol-gel transition temperatures of the hydrogels. The thermoreversibility of the formulations allowed facile loading in the microwell. Warming the formulations at 30°C rapidly increased their viscosities to promote bulk formation on the microneedle surface (Figure 1A). Up to 2.5  $\mu\text{g}$  MB was loaded per 1  $\text{cm}^2$  microneedle patch. Whilst uncoated MB-poloxamer formulations exhibited extended release characteristics in vitro, coated formulations showed rapid release characteristics, probably due to the smaller bulk of the coating in the latter. The microneedles released MB within 15 min when inserted into porcine skin (Figure 1B).

## Conclusion

Thermoreversible hydrogel formulations enable on-the-fly, temperature-controlled manipulation of formulation viscosity. This strategy can be used to formulate microneedle drug coatings for minimally invasive drug delivery in the skin.

## References

- [1] R. Haj-Ahmad, H. Khan, M. Arshad, M. Rasekh, A. Hussain, S. Walsh, et al., “Microneedle coating techniques for transdermal drug delivery” *Pharmaceutics*, 7 (2015) 486–502.
- [2] S.-J. Kim, J.-H. Shin, J.-Y. Noh, C.-S. Song and Y.-C. Kim, “Development of the novel coating formulations for skin vaccination using stainless steel microneedle” *Drug Deliv. Transl. Res.*, 6 (2016) 486–97.

- [3] K.W. Ng, W.M. Lau and A.C. Williams, “Towards pain-free diagnosis of skin diseases through multiplexed microneedles: biomarker extraction and detection using a highly sensitive blotting method” *Drug Deliv. Transl. Res.*, 5 (2015) 387–396.